Amendments to the Drawings:

The attached sheet of drawings includes one change to Fig. 4. This sheet, which includes Figs. 2 and 4, replaces the original sheet including Figs. 2 and 4. In Fig. 4, a reference numeral, 40, has been added to indicate the "sample chamber" in Fig. 4. This same reference numeral 40 was added in the specification, specifically, at page 10, line 30.

Attachment: Replacement Sheet
Annotated Sheet Showing Changes

REMARKS

Favorable reconsideration and allowance of the present application are respectfully requested in view of the foregoing amendments and the following remarks.

Currently, claims 46-61 are pending in the present application, including independent claim 46. Minor amendments have been made to claims 48, 57, and 61 in this paper.

Independent claim 46, for instance, is directed to a method for detecting the presence of a proteinase enzyme in a chronic wound of a human or an animal. The method comprises collecting a sample of fluid from the chronic wound of the human or the animal. The sample is exposed to a signal element bound to a target antibody, the target antibody being bindable to the proteinase enzyme to form a proteinase enzyme/target antibody complex. The proteinase enzyme/target antibody complex is exposed to a capture antibody to form a proteinase enzyme/target antibody complex/capture antibody conjugate. The proteinase enzyme is identified by determining the presence or absence of a detectable or measurable manifestation of the signal element. This identification allows for the selection of a treatment for the chronic wound that is effective for treating the identified proteinase enzyme.

As an initial matter, at page 2, the Office Action objected to the "Brief Description of the Drawings" section of Applicants' specification. Specifically, the Examiner stated that "the public should not have to search through the specification for" explanation of the figures and that the "Brief Description of the Figures should define all labeling in the figures." Accordingly, Applicants have amended several paragraphs of the

specification, as shown at pages 2-4 of this paper, in order to comply with the Examiner's request.

In the Office Action, dependent claims 48-50 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants have amended claim 48 in this paper to recite that the target antibody and the signal element are "bound" to a particle. However, claim 48 is not intended to distinguish "whether the signal element and antibody are both bound directly, and independently to the particle or whether the signal element is bound to the antibody and the signal element/antibody complex is bound to the particle," as set forth on page 2 of the Office Action.

Claim 48 simply describes the target antibody and the signal element as both being "bound to" a particle, which can occur in various ways as described throughout Applicants' specification. By way of example only, page 8, lines 6-13 state that the "antibody and the signal element can be coupled to a particle by one of several chemical methods known to those skilled in the art," going on to describe, for instance, a carbodiimide chemical method. Likewise, page 8, lines 22-26 state that "target antibodies can be disposed within the sample reservoir upon a particle including, but not limited to, latex, polymers, gold, silicon, glass, metal, bacterial or fungal cells, or any particle to which the signal element and target antibody can be attached by any method known in the art." Similarly, page 14, lines 10-11 describe procedures occurring during Example 1, wherein "target antibodies were affixed to carboxylated polystyrene beads of 0.3 micron diameter pre-labeled with a blue dye." In all of these portions of the specification, Applicants make clear that the target antibody and the signal element both being "bound to" a particle, as stated in Claim 48, can occur in several different, yet

acceptable, ways. Thus, Applicants respectfully submit that the pending claims fulfill the requirements of 35 U.S.C. § 112.

Additionally, in the Office Action, independent claim 46 was rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,736,341 to Sorsa, et al. Sorsa, et al. is directed to a method and test kit for diagnosing periodontal disease. Specifically, in Sorsa, et al., monoclonal antibodies are used to recognize the active form of mammalian MMP-8 and differentiate between the active and proenzyme forms. Sorsa, et al. also describes exemplary test kits for diagnosing periodontal disease. (See e.g., Cols. 21-22).

However, the method for diagnosing periodontal disease taught in Sorsa, et al. does not disclose the presently claimed method for detecting the presence of a proteinase enzyme in a chronic wound of a human or an animal. Sorsa, et al. is specific to the use of a saliva sample, a mouthrinse sample, or a sample of gingival crevicular fluid (GCF) to diagnose whether or not a patient has periodontal disease.

In contrast, the presently claimed method involves the step of collecting a sample of fluid from a chronic wound of a human or an animal. The accepted clinical definition of a "chronic wound" does not include oral lesions or periodontal diseases that result in bleeding. Rather, these oral lesions resulting from gum disease are defined as "acute" wounds that may worsen without treatment. Chronic wounds and acute wounds are characterized by different sets of biochemical pathway disturbances, and although MMPs may be associated with both chronic wounds and gum disease, the two are quite distinct biochemically.

"Chronic wounds" include, by way of example, open cutaneous wounds, burn wounds, neuropathic ulcers, pressure sores, venous stasis ulcers, and diabetic ulcers, as described at page 1 of Applicants' specification. And chronic wounds are characterized by an increase in the activity of proteinase enzymes such as MMPs. These enzymes are responsible for the continued degradation of newly formed basal extracellular matrix (ECM).

The stable formation of the ECM marks a committed entry into the healing process; however, constant ECM turnover results in an inability of the chronic wound to heal. Under normal circumstances, MMPs are prevented from destroying the wound bed by the action of tissue inhibitors of metalloproteinases (TIMPs). In chronic wounds, however, the ratio of MMP to TIMP is high, such that most of the MMPs are uninhibited. In fact, with elevated proteinase enzyme levels, the TIMP molecules themselves can be hydrolyzed. (Appl., pp. 1-3).

As such, chronic wounds may be treated with inhibitory agents. Unfortunately, no naturally occurring TIMP molecule is known that inhibits all types of MMPs. TIMPs instead form inhibitory complexes with only a specific subset of MMPs. Thus, for therapeutic purposes, it is desirable to specifically identify which proteinase enzyme is present in the chronic wound. Further, because the levels of the proteinase enzymes are constantly in flux within a chronic wound, it is also desirable to identify the proteinase enzyme in the *current* condition of the chronic wound. (Appl., pp. 1-3).

In this regard, the presently claimed invention provides for a fast, accurate, and inexpensive method for detecting the presence of one or more specific proteinase enzymes in a sample of fluid taken from a chronic wound. This rapid detection allows

for immediate treatment with an inhibitory agent that is specific for the identified proteinase enzyme. Advantageously, the inhibitory agent that is specific for the identified proteinase may be used to treat the *current* condition of the wound, without having to wait several days for the result.

Sorsa, et al. simply fails to disclose the claimed method for detecting the presence of a proteinase enzyme in a "chronic wound." Indeed, having an MMP sensor for detecting gum disease in no way teaches that such a sensor could be useful in chronic wound therapeutics Thus, for at least the reasons set forth above, Applicants respectfully submit that the present claims patentably define over Sorsa, et al.

Independent claim 46 was also rejected in the Office Action under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 6,143,506 to Golub, et al. However, Golub, et al. suffers from the same deficiencies noted above with respect to Sorsa, et al. That is, Golub, et al. is directed to a method for diagnosing periodontal disease, but fails to disclose the claimed method for detecting the presence of a proteinase enzyme in a "chronic wound." For at least this reason, Applicants respectfully submit that the present claims patentably define over Golub, et al.

Dependent claims 47-61 were also rejected under one or both of the above-discussed references and/or the Rowe, et al. and Vu, et al. articles. Applicants respectfully submit that at least for the reasons indicated above relating to independent claim 46, dependent claims 47-61 patentably define over the reference(s) cited. However, Applicants also note that the patentability of dependent claims 47-61 does not necessarily hinge on the patentability of independent claim 46. In particular, some or all

of dependent claims 47-61 are believed to possess features that are independently patentable, regardless of the patentability of independent claim 46.

As such, at least for the reasons set forth herein, Applicants respectfully submit that the present application is in complete condition for allowance and favorable action, is therefore requested. Examiner Swope is invited and encouraged to telephone the undersigned, however, should any issues remain after consideration of this Amendment.

Please charge any additional fees required by this Amendment to Deposit Account No. 04-1403.

Respectfully requested,

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